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A randomised controlled trial of prednisone versus placebo in the management of human immunodeficiency virus (HIV)-infected patients presenting with mild to moderate Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome after commencing Highly Active Antiretroviral Therapy

Submission date
03/06/2005

Recruitment status
No longer recruiting

Registration date
17/08/2005

Overall study status
Completed

Last Edited
17/08/2012

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
TB-IRIS-RCT

Study information

Scientific Title

Acronym
TB-IRIS-RCT

Study objectives
We propose a randomised placebo-controlled trial of prednisone as an adjunct in the management of HIV-infected patients with mild to moderate Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome (TB-IRIS). This syndrome manifests as a paradoxical worsening of clinical features of tuberculosis after commencing Highly Active Antiretroviral Therapy (HAART). We hypothesise a reduction in the requirement for hospitalisation and therapeutic procedures among patients receiving prednisone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
HIV and Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome

Interventions
Randomization to oral prednisone 1.5 mg/kg for 2 weeks followed by 0.75 mg/kg for 2 weeks or identical placebo medication.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Prednisone

Primary outcome measure
Combined hospitalisation and procedures endpoint (cumulative duration of hospitalisation in days + outpatient therapeutic procedures counted as one day)

Secondary outcome measures
Radiological Endpoints:
A significant improvement in radiological manifestations of IRIS:
1. For Chest X Ray pulmonary infiltrates, a significant reduction in composite infiltrate score (6 zones each measured for degree of infiltrate by Radiologist to give composite score)
2. For large nodes noted on the Chest X Ray, a significant reduction in size
3. For computed tomography (CT) scans, a significant reduction in infiltrate or node size
4. For peripheral & abdominal nodes, a significant reduction in volume as measured by ultrasound
5. For cold abscesses, a significant reduction in volume as measured by ultrasound

Other Secondary Endpoints:
1. 50% reduction in symptom score (Wilson 2004)
2. A significant improvement in the Quality of Life MOS-HIV score
3. Improvement in Karnofsky score of greater than 10
4. Corticosteroid side effects
a. New onset of diabetes
b. New onset of hypertension
c. Psychological side effects
d. Onset of new opportunistic infection/cancer such as Kaposis sarcoma, Herpes simplex lesions, Herpes zoster lesions
5. 50% reduction in C-Reactive Protein (CRP) value
6. Weight gain
7. Mortality
8. The need to stop HAART, TB therapy or study drug
9. Adherence with HAART and study drug as assessed by pill count and adherence with TB treatment as assessed by TB clinic card assessment
10. Recurrence of IRIS manifestations within the 12 week study period
11. In patients with an Alkaline Phosphatase or gamma glutamyl transpeptidase (GGT) that was elevated more than 2 x upper limit of normal (ULN) at baseline, a reduction of 50% from the baseline value
12. CD4 and Viral load
13. For ascites, reduction in abdominal girth

Overall study start date
01/06/2005

Completion date
31/05/2007

Eligibility

Key inclusion criteria
A. Age 18 years and over

B. Informed consent (written)

C. Prior to the introduction of HAART the following criteria must be met for the diagnosis of TB-IRIS to be considered:
1. The patient has HIV infection
2. The patient should be antiretroviral-naïve (excluding receipt of antiretroviral treatment within mother to child transmission programmes Nevirapine single-dose with or without Zidovudine in the third trimester)
3. The patient has microbiologic, histologic or very strong clinical evidence of tuberculosis
4. There has been a documented improvement in symptoms, Karnofsky score and/or weight, resolution of fever and clinical and radiological stabilization during the intensive phase of multidrug TB therapy
5. That adherence with anti-TB treatment is >80%
6. That the infecting strain of M. tuberculosis is sensitive to rifampicin, if this result is available

D. Consider TB-IRIS if, within 3 months of the introduction of multi-drug HAART
1. Adherence with HAART is documented and the patient was on anti-tuberculous therapy when HAART commenced
2. There are new or recurrent constitutional symptoms PLUS one or more of:
i. New or expanding lymph nodes (>20 mm or >50% in volume)
ii. New or expanding tuberculous cold abscesses (e.g. paraspinal)
iii. New or expanding pulmonary infiltrates (radiographically confirmed)
iv. New or enlarging serous effusions (pericardial, pleural or ascitic)
Patients presenting with other manifestations of TB-IRIS (e.g. central nervous system [CNS] tuberculoma) will not be included in this study.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

100

Key exclusion criteria
1. Previous systemic steroid therapy as part of the management of tuberculosis
2. Pregnancy
3. Uncontrolled Diabetes Mellitus
4. Adrenal failure
5. Severe TB-IRIS (these cases will receive open label corticosteroids) manifested by:
a. Respiratory failure (pO2 <8 kPa)
b. Altered level of consciousness or new focal neurological signs
c. Compression of vital structures (e.g. bronchostenosis)
6. Kaposis sarcoma

Date of first enrolment
01/06/2005

Date of final enrolment
31/05/2007

Locations

Countries of recruitment
South Africa

Study participating centre
Division of Pharmacology
Cape Town
South Africa
7925

Sponsor information

Organisation
University of Cape Town - Research Ethics Committee, Faculty of Health Sciences (South Africa)

Sponsor details
Research Ethics Committee
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Sponsor type

University/education

ROR
https://ror.org/03p74gp79

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council, South Africa (no reference number provided)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/08/2012		Yes	No